Outcomes After Surgery and Radiotherapy for Papillary Tumor of the Pineal Region

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■ BACKGROUND: **Papillary tumor of the pineal region (PTPR) is a rare neuroectodermal tumor that was first described in 2003 and formally codified by the World Health Organization in 2007. Limited reports suggest surgical resection is the mainstay of treatment; however, the role of multimodality therapy is not well defined. We evaluated our institutional experience in the treatment of PTPR.**

■ METHODS: **A retrospective review of 8 patients with pathologically confirmed PTPR diagnosed between 1999 and 2013 was performed.**

■ RESULTS: **The median age at diagnosis was 37 years (range, 25–56 years). After a median follow-up period of 60 months (range, 10–170 months), 7 of 8 patients were still living. All patients underwent maximum safe surgical resection; 5 received adjuvant radiation (63%). Overall and progression-free survival 5 years after diagnosis were 100% and 51%, respectively. Progression-free survival 5 years after completion of adjuvant radiotherapy was 64%. Crude recurrence rates for patients receiving adjuvant radiotherapy ($n = 5$) and patients not receiving adjuvant radiotherapy ($n = 3$) were 20% and 67%, respectively. Crude recurrence rate after gross total resection (GTR) and no adjuvant radiotherapy ($n = 2$) was 100% versus 0% when adjuvant radiotherapy was administered after GTR ($n = 2$). After subtotal resection, 3 patients received adjuvant radiotherapy; 1 of these patients had out-of-field recurrence at 46 months (crude recurrence rate 33%). In all cases, salvage with radiation at the time of recurrence was effective.**

■ CONCLUSIONS: **Our institutional experience confirms a recent multicenter retrospective series showing excellent survival but high risk of local recurrence for PTPR. Our findings suggest that radiotherapy provides durable local control, particularly when administered in the adjuvant setting after GTR.**

INTRODUCTION

Pineal region tumors are rare, comprising approximately 1% of all intracranial neoplasms (4). Tumors that form in this area are diverse in origin, potentially arising from pineal parenchymal cells, pineal cysts, germ cells, ependymal cells, glial cells, the meninges, and metastases. Papillary tumors of the pineal region (PTPR) were described more recently as a distinct histopathologic entity of tumors in this region. PTPR are tumors of neuroectodermal origin that arise from specialized ependymal cells of the subcommissural organ and were first described in 2003 and formally codified by the World Health Organization in 2007 (10, 12).

Maximum safe surgical resection is the suggested first-line treatment for PTPR; however, because of the paucity of reported cases, it is difficult to establish a role for adjuvant treatment. The largest reported series of patients with histopathologically confirmed PTPR consists of 44 patients from multiple centers across Europe and Japan (5). Of these patients, 64% received radiotherapy, and 18% received chemotherapy; however, it is unclear whether radiotherapy was delivered in the adjuvant setting or in the setting of recurrent disease. We previously reported the clinical and histopathologic findings of 3 patients

Key words
- Pineal region tumor
- Radiation
- Surgery

Abbreviations and Acronyms
GTR: Gross total resection
HPF: High-power field
MRI: Magnetic resonance imaging
PFS: Progression-free survival
PTPR: Papillary tumor of the pineal region
SRS: Stereotactic radiosurgery
STR: Subtotal resection

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treated for PTPR at our institution (3). In the present study, we performed a retrospective review of our institutional experience of 8 patients with a diagnosis of PTPR and a median follow-up period of 5 years.

MATERIALS AND METHODS

Patients

After obtaining permission from the institutional review board, we retrospectively identified all patients with PTPR whose histopathology was reviewed by a neuropathologist from our institution. Anatomic location and morphologic and immunophenotypic features were used to establish pathologic diagnosis according to current World Health Organization criteria (12). In addition to assessing specimens for characteristic histologic features, commonly examined markers included cytokeratins, S100, CAM 5.2, and epithelial membrane antigen. Mitotic activity was determined by counting mitoses in 10 high-power fields (HPF) or assessing proliferation using immunohistochemistry and automated quantitation of phosphohistone H3 or Ki-67/MIB-1. In the absence of documented mitoses per 10 HPF, mitotic activity was assigned an arbitrary numerical value based on pathologic report of absent, single, rare, or occasional mitotic figures.

There were 8 patients identified, 1 of whom received counseling at our institution but treatment at an outside institution. Work-up consisted of a complete history and physical examination and preoperative craniospinal magnetic resonance imaging (MRI). Extent of surgical resection was determined based on operative reports and postoperative imaging. Data on clinical course and any subsequent treatment were collected via chart review and updated until last follow-up visit or death. In the absence of clinical follow-up, information on patient vital status was collected using our institutional tumor registry, which obtains patient data with annual phone calls, letters, and review of records from the Bureau of Vital Statistics.

Data Analysis

Disease and toxicity-related outcomes were evaluated. Overall survival and progression-free survival (PFS) were calculated from the date of diagnosis and from the end of radiation treatment using the Kaplan-Meier algorithm. PFS was defined as a patient alive without local, regional, or distant recurrence. Patients were censored at last follow-up visit or clinical correspondence or death. Statistical analysis was performed using Stata/MP 13.1 (StataCorp LP, College Station, Texas, USA).

RESULTS

Patient and Treatment Characteristics

Patient characteristics are listed in **Table 1**. Median age at diagnosis was 37 years (range, 25–56 years). There were 4 women and 4 men. There were 6 white patients and 2 Hispanic patients. The most common presenting symptoms were deficits in ocular motility, headache, and short-term memory deficits. Hydrocephalus was noted in all cases. Magnetic resonance imaging (MRI) showed tumors located in the pineal region with extension into the third ventricle in 3 cases, extension into the fourth ventricle in 1 case, and involvement of the thalamus by a cystic component in 1 case. Median maximum tumor diameter was 2.9 cm (range, 1.1–4.5 cm). As previously described (2, 3), all tumors exhibited heterogeneous enhancement on T1 postcontrast imaging, and most (75%) had cystic components.

Table 1. Summary of Patient Characteristics

Variable	
Follow-up (months)	
Median (range)	60 (10–170)
Age (years)	
Median (range)	37 (25–56)
Sex	
Male	4 (50%)
Female	4 (50%)
Ethnicity	
White	6 (75%)
Hispanic	2 (25%)
Tumor size (cm)	
Median (range)	2.9 (1–4.5)
Presenting signs and symptoms	
Hydrocephalus	8 (100%)
Headache	5 (63%)
Visual defects	6 (75%)
Short-term memory deficits	4 (50%)
Extent of resection	
STR	4 (50%)
GTR	4 (50%)
Number of surgeries	
1	6 (75%)
2	2 (25%)

Data are presented as number (percent) unless otherwise noted.
STR, subtotal resection; GTR, gross total resection.

Gross total resection (GTR) was achieved in 4 patients (50%). The remaining 4 patients had a subtotal resection (STR); 2 of these patients initially underwent third ventriculostomy and biopsy at outside institutions before definitive surgery at our institution. Surgical approaches for resection included supracerebellar-infratentorial ($n = 3$), interhemispheric-transventricular ($n = 4$), and endoscopic transventricular ($n = 1$).

Radiotherapy was administered to 7 patients (88%), either in the adjuvant ($n = 5$; 63%) or recurrent ($n = 2$; 25%) settings. Only 1 patient—who had significant cognitive and linguistic deficits after surgery—did not receive radiation. This patient was lost to follow-up 10 months after surgery. In the adjuvant setting, radiotherapy was delivered 2–9 weeks after surgery and consisted of whole-brain radiotherapy ($n = 1$); stereotactic radiosurgery (SRS) ($n = 2$); proton radiotherapy to the surgical bed ($n = 1$); and whole